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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/611,593 | 06/30/2003 | Marie-Laure Lesaicherre | 6565-66285/RJP | 5201 |

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| EXAMINER | |
|---|---|
| YANG, NELSON C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/611,593 | LESAICHERRE ET AL. | |
| | Examiner | Art Unit | |
| | Nelson Yang | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4 and 6-20* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 11, 2008 has been entered.

### *Response to Amendment*

2. Applicant's amendment of claims 1, 2, 4, 6, 9-10, 13, 16 is acknowledged and has been entered.

3. Applicant's cancellation of claim 5 is acknowledged and has been entered.

4. Claims 1-4, 6-16 are currently under examination.

5. Claims 17-20 are withdrawn.

### *Rejections Withdrawn*

6. Applicant's arguments, see amended claims, filed June 11, 2008, with respect to the rejection of claims 1-3, 9, and 10 under 35 U.S.C. 102(b) as being anticipated by Nock et al. [US 2002/0049152] have been fully considered and are persuasive. The rejection of claims 1-3, 9, and 10 under 35 U.S.C. 102(b) as being anticipated by Nock et al. [US 2002/0049152] has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view

of Eaton et al.[ Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196] as discussed below.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-3, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196].

With respect to claims 1, 9, Nock et al. teach a method of immobilizing a polypeptide to a surface using mutant inteins (para. 0045) comprising cysteine, serine or threonine (para. 0057), wherein the amino-terminal end of the intein is capable of splicing of the N-extein to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0057-0059). Specifically, Nock et al. teach expressing a chimeric gene that encodes a fusion protein which comprises a polypeptide and an intein (para. 0013), attaching anchor molecules to the polypeptides and anchoring the polypeptides to a surface (para. 0014). Nock et al. fail to teach that the cysteine is biotinylated.

Eaton et al., however teach that biotinylated cystein acts as a probe for thiolated proteins, which are detected using non-reducing Western blots probed with streptavidin horseradish

peroxidase. Nock et al. also teach that tags may be used to attach the polypeptides to the surface to form arrays or for purification of the polypeptides (para. 0065), wherein the tags may be avidin (claim 12), which would bind to biotin.

Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to use a biotinylated cysteine to splice the fusion protein of Nock et al., as suggested by Eaton et al., as this would allow for the following step of detection of the thiolated polypeptide such as with the use of non-reducing Western blots probed with streptavidin horseradish peroxidase. This would also accomplish the goal of allowing the polypeptides to be attached to the surface of an array using avidin tags.

9. With respect to claims 2, 10, Nock et al. teach that tags may be used to attach the polypeptides to the surface to form arrays or for purification of the polypeptides (para. 0065), wherein the tags may be avidin (claim 12), which would bind to biotin.

10. With respect to claim 3, the substrate of the array may be glass (para. 0119).

11. Claims 4, 11 are rejected under 35 U.S.C. 103(a) as being unpatentable Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196], as applied to claims 1, 9 above, and further in view of Duan [US 6,951,742].

With respect to claims 4, 11 Nock et al. teach a method of immobilizing a polypeptide to a surface using mutant inteins (para. 0045), wherein the amino-terminal end of the intein is capable of splicing of the N-extein to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0059). Specifically, Nock et al. teach expressing a chimeric gene that encodes a fusion protein which comprises a polypeptide and an intein (para.

0013), attaching anchor molecules to the polypeptides and anchoring the polypeptides to a surface (para. 0014). Nock et al. fail to teach that the proteins are expressed by a pTYB1 expression vector.

Duan, however, teaches the use of pTYB1 vectors to express fusion proteins, and further teach that pTYB1 vectors allow the cloning of a target gene immediately adjacent to the intein cleavage site, which results in the purification of a native target protein without any vector derived extra residues after the cleavage (column 32, lines 52-65).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use a pTYB1 expression vector to express the fusion proteins of Nock et al., as suggested by Duan, in order to allow the cloning of a target gene immediately adjacent to the intein cleavage site, allowing for the purification of a native target protein without any vector derived extra residues after the cleavage.

12. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196], as applied to claim 2 above, and further in view of Bradley et al. [US 2002/0006623].

With respect to claims 6, 7, Nock et al. teach a method of immobilizing a polypeptide to a surface using mutant inteins (para. 0045), wherein the amino-terminal end of the intein is capable of splicing of the N-extein to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0059). Specifically, Nock et al. teach expressing a chimeric gene that encodes a fusion protein which comprises a polypeptide and an intein (para. 0013), attaching

anchor molecules to the polypeptides and anchoring the polypeptides to a surface (para. 0014). Nock et al. fail to teach that the glass support is derivatized with an epoxy silane compound such as glycidoxypropyl trimethoxysilane.

Bradley et al., however, teach the dervizatization of glass supports with glycidoxypropyl trimethoxysilane (para. 0127), and further teach that glycidoxypropyl trimethoxysilane is rapid, and occurs under very mild conditions using a minimum of inexpensive reagents (para. 0128).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have derivatized the glass supports of Nock et al. with glycidoxypropyl trimethoxysilane, as suggested by Bradley et al., in order to be able to attach ligands to the glass support rapidly, and under very mild conditions while using a minimum of inexpensive reagents, which would render it cheaper, quicker, and simpler that other methods.

13. With respect to claim 8, Nock et al. teach streptavidin (claim 12).

14. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196] and in view of Duan [US 6,951,742] as applied to claim 11 above, and further in view of Inoue et al. [US 2002/0123101].

With respect to claim 12, Nock et al. teach a method of immobilizing a polypeptide to a surface using mutant inteins (para. 0045), wherein the amino-terminal end of the intein is capable of splicing of the N-extein to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0059). Specifically, Nock et al. teach expressing a chimeric gene that

encodes a fusion protein which comprises a polypeptide and an intein (para. 0013), attaching anchor molecules to the polypeptides and anchoring the polypeptides to a surface (para. 0014). Nock et al. fail to teach that or that the fusion protein is contacted with a chitin column.

Inoue et al., however, teach that chitin column are commonly used for purification of proteins. (para. 0217).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention for Kurz et al. and Duan to have the fusion proteins come in contact with a chitin column, in order to purify the protein, as suggested by Inoue et al., so that there would be no contaminants that would potentially interfere and contaminate the protein array, thus allowing for better quality in the protein arrays produced.

15. Claims 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196], Duan [US 6,951,742] and Inoue et al. [US 2002/02123101], as applied to claim 12 above, and further in view of Xu et al. [US 7,001,745].

With respect to claim 13, Nock et al. teach a method of immobilizing a polypeptide to a surface using mutant inteins (para. 0045), wherein the amino-terminal end of the intein is capable of splicing of the N-extein to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0059). Specifically, Nock et al. teach expressing a chimeric gene that encodes a fusion protein which comprises a polypeptide and an intein (para. 0013), attaching

anchor molecules to the polypeptides and anchoring the polypeptides to a surface (para. 0014). Nock et al. fail to teach adding the cystein-biotin to a chitin column.

Xu et al., however, teach that the chitin column allows for tagged proteins to be isolated during ligation procedures (column 6, lines 35-45).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have used a chitin column in the method of Nock et al., in order to allow the biotin-cysteine tagged polypeptides of Nock et al. to be isolated from the rest of the composition.

16. With respect to claim 14, Nock et al. teach substrates comprising glass (para. 0119).

17. With respect to claim 15, Nock et al. teach streptavidin (claim 12).

18. With respect to claim 16, Duan teaches spotting the protein onto a solid surface to form an array (column 37, lines 1-25).

***Response to Arguments***

19. Applicant's arguments with respect to claims 1-4, 6-16 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

20. No claims are allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Patent Examiner, Art Unit 1641